

Abstract

The invention relates to a vaccine comprising a bacterium attenuated by a non-reverting mutation in a gene encoding a protein which promotes folding of extracytoplasmic proteins. Such mutations were initially identified as being useful in vaccines from a bank of randomly inserted, transposon mutants in which attenuation was determined as a reduction in virulence of the organism in the mouse model of infection. Site directed mutation of the gene results in a strain which shows at least 4 logs of attenuation when delivered both orally and intravenously. Animals vaccinated with such a strain are protected against subsequent challenge with the parent wild type strain. Finally, heterologous antigens such as the non-toxic and protective, binding domain from tetanus toxin, fragment C, can be delivered via the mucosal immune system using such strains of bacteria. This results in the induction of a fully protective immune response to subsequent challenge with native tetanus toxin.